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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/882,415	06/25/97	ZHANG S	MIT-7762

HM12/0508
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EXAMINER	
GARCIA, M	
ART UNIT	**PAPER NUMBER**
1627	19

DATE MAILED: 05/08/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/882,415	Zhang et al
Examiner	**Group Art Unit**
Maurie E. Garcia, Ph. D.	1627

☒ Responsive to communication(s) filed on *Feb 28, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *THREE* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-21* is/are pending in the applicat

Of the above, claim(s) *20 and 21* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-19* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Please note: The number of Art Unit 1618 has been changed to 1627. Please direct all correspondence for this case to **Art Unit 1627**.

1. In view of the appeal brief filed on February 28, 2000, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(a) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(b) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

2. Pursuant to a conversation with Mr. David Brook (see attached Interview Summary form), the After Final amendment filed September 1, 1999 has **not** been entered and the claims examined below are those pending as of the amendment of January 11, 1999 (Paper No. 8). Currently, claims 1-21 are pending and claims 1-19 are examined.

3. The finality of the previous Office Action is withdrawn in view of the new grounds of rejection stated in this Office Action.

Restriction/Election

4. Please note that this application contains claims 20 and 21 drawn to an invention nonelected with traverse in Paper No. 8. As stated by the previous examiner, the restriction requirement will be revisited at a later time provided the presently elected claims become allowable.

Claim Objections

5. Claims 1, 16, 18 and 19 are objected to because of the following informalities: It appears that the word "are" is missing between "said peptides" and "bound directly". Appropriate correction is required.

New Grounds of Rejection
Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a monolayer of peptide bound in the relief pattern

of a pre-printed substrate, does not reasonably provide enablement for direct microcontact printing of peptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It is clear from applicant's specification how one might practice this invention when a monolayer of peptide is bound in the relief pattern of a pre-patterned substrate (or bound to pre-patterned molecules); however, there is insufficient guidance as to how to perform direct patterning of peptides. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims: The claim states broad methodology for printing a pattern of peptides using a stamp. The nature of the invention: The invention is a method for preparing a patterned monolayer of peptides using a stamp and the claim gives only broad method steps. The state of the prior art and the level of predictability in the art: While self-assembled monolayers and even patterning of

monolayers by stamping (referred to in the art as microcontact printing), were well known at the time of filing, there were only a few examples of different molecules used for patterning ("inking" the stamp) and to the examiner's knowledge, there were no examples at the time of filing of direct microcontact printing of peptides. The interaction of the "inking" compound and the stamp is crucial to the formation of good patterns, and is not predictable, as taught by Zhang et al (Biomaterials 1999, Vol. 20, pages 1213-1220. See page 1218, bottom). The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. The amount of direction provided by the inventor and the existence of working examples: Applicants have only provided one working example, which is of indirect printing. That is, the peptides are bound in the relief pattern of a pre-patterned molecule. The specification gives no guidance as to the conditions that would be needed to be able to directly print the peptides as claimed. The quantity of experimentation needed to make or use the invention based on the content of the disclosure: It would require undue experimentation to determine the conditions necessary to be able to directly print patterns of peptides by the claimed method due to the lack of guidance of the instant specification. One may need to use a special elastomer for the stamp and/or the stamp may need pretreatment, as taught by Zhang et al. Also, further research would be needed to determine the proper solvent to achieve the correct wetting conditions for monolayer formation by direct stamping.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 8, 12 and 16 -19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claims 1, 16, 18 and 19 the term "predetermined" is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. While the instant specification defines what is meant by patterned (page 12: "having ordered areas where the peptides are and are not bound"), the procedure by which the patterns are "predetermined" is not clear.

B. In claims 1, 16, 18 and 19 the term "bound directly" renders the claims indefinite because it is unclear what exactly the phrase means in this context. It appears that applicant is using this phrase to mean two separate things: (1) physical attachment of the peptide to the solid support with no intermediary compounds between the peptide and the solid support and (2) attachment to a solid support via a terminal amino acid (no additional functionality added to the peptide), whether or not an intermediary compound is present. This makes the instant claims extremely confusing. See also paragraphs 12 & 22.

C. Claim 8 is indefinite because it is unclear whether the "functional group" can be attached to the amino or carboxy group of the terminal amino acid. The way the claim is written makes it appear that a functional group can be pendant from a side chain **or** amino **or** carboxy group of a terminal amino acid and therefore modified peptides would be encompassed by the claim. This also adds to the confusion discussed in B. above since "bound directly" can be interpreted to mean no additional functionality added to the peptide. If this is the case, the functional group as recited in claim 8 could not be present in a peptide that is "bound directly".

D. Claim 12 is unclear in the recitation of "about 2 to about 50 amino acids". Since there is no way to have a fraction of an amino acid, it is unclear if this phrase is meant to encompass values such as 1 amino acid or 51 amino acids or simply means from 2-50 amino acids.

E. Claim 16 is unclear in the recitation of "at least about 2". Since there is no way to have a fraction of an amino acid, it is unclear if this phrase is meant to encompass 1 amino acid or simply means 2 or more.

F. Claim 17 recites that the chemical reactive moiety is linked to "said solid support through one or more peptide linkages". This renders the claim indefinite because it is unclear what applicant intends the linkage between the solid support and the moiety to be. One of ordinary skill would interpret "peptide linkage" to mean an amide bond and the direct formation of an amide linkage between the moiety and the solid support is impossible unless other intermediary compounds

are used to derivatize the support. Even if intermediary compounds were used to derivatize the solid support and then a covalent amide linkage was made (a procedure which is well known in the art), it is completely unclear how this would fit the definition of self-assembled (see instant specification page 2, lines 4-7). Additionally, the recitation of one *or more* (emphasis added) linkages is also indefinite. It appears that there cannot there be more than one linkage to the support for this type of self assembled monolayer. For the purposes of applying the prior art, the examiner has interpreted this phrase as set forth below in paragraph 11.

New Grounds of Rejection
Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-3, 6, 8-11 and 17 are rejected under 35 U.S.C. 102(b) as anticipated by Duschl et al (Reference AT3 on Applicant's PTO-1449).

Duschl et al teach "the fabrication of patterns with contrasting surface properties on gold substrates" (see Abstract). Self-assembled monolayers of peptides are formed in a pattern having ordered areas where the peptides are and

are not bound, as shown in Figure 1B and Figure 3. The patterns are determined by the properties of the mixture of palmitic acid and sulfur-bearing lipid (page 1229, 2nd column). The "patterned surface for the differential binding of proteins" (see page 1233, 2nd column) is formed by linear peptides containing a terminal cysteine group, which reads directly on claims 8-11. The peptides are directly bound to a gold substrate by the interaction of the thiol sidechain with the surface. The peptides have the structure $CY(NANP)_3$ – with C being the terminal reactive group (terminal amino acid), Y the central linker and $(NANP)_3$ the presenting group (see pages 1230-1231).

Note that in claim 17, the phrase "one or more peptide linkages" is deemed to be unclear by the examiner (see Paragraph 9F above). For the sake of this rejection, the examiner is interpreting this to mean a one linkage of the peptide to the solid support with no intermediary compounds involved, as in the linkage of the terminal cysteine to the gold as taught by Duschl et al.

12. Claims 1-3, 5 and 18 are rejected under 35 U.S.C. 102(b) as anticipated by Lopez et al (Reference AX2 on Applicant's PTO-1449).

Note: applicant's response dated January 11, 1999 (Paper No. 8) states that two methods are disclosed for patterning the peptide monolayers. Beginning on the bottom of page 8:

"In the first method, a solid support which will not bind the peptide is coated in a predetermined pattern with a compound that will bind the terminal reactive group of the peptide. The compound is deposited on the solid support in a predetermined pattern using a stamp. Then the solid support

is contacted with a solution of the peptide which then binds to the compound in the predetermined pattern."

The method of Lopez et al reads directly on this method, as elaborated below. See also Paragraph 22.

Lopez et al teach patterns of proteins adsorbed on a self-assembled monolayer (SAM) on gold (see page 10775 and Figure 1b). The proteins are adsorbed to a monolayer of CH_3-terminated SAM as described on pages 10776-10777 (in section titled "Spatial Patterning of Adsorbed Proteins"). These monolayers are patterned in a variety of ways, most importantly, by the stamping method of the instant invention (see Figure 1c and accompanying caption/text). Furthermore, supports having two different peptides are also taught (see Figure 7 and section titled "Comparative Imaging of Different Adsorbed Proteins").

13. Claims 1-4, 6 and 8-10 are rejected under 35 U.S.C. 102(b) as anticipated by Knichel et al (Reference AU3 on Applicant's PTO-1449).

Knichel et al teach a self assembled monolayer of peptides on a patterned substrate (see Abstract and Figure 3). Specifically the substrate is glass with gold electrodes patterned thereon. The thiol-modified peptide (see Figure 1) adheres only to the gold coated portions of the substrate (i.e. the pattern is the pattern of the underlying gold electrode; the peptides are not bound to the uncoated glass portions). As shown in Figure 1, the peptide has a terminal amino acid of arginine and a thiol terminal reactive group.

Note that in claim 8, the terminal reactive group can be interpreted as being pendant from a side chain **or** amino **or** carboxy group of a terminal amino acid and therefore modified peptides would be encompassed by the claim. For the sake of this rejection, the examiner is interpreting the claims to mean that the terminal reactive group is a functional group pendant to the amino terminus of the peptide. See Paragraph 9C above.

New Grounds of Rejection
Claim Rejections - 35 USC § 102/103

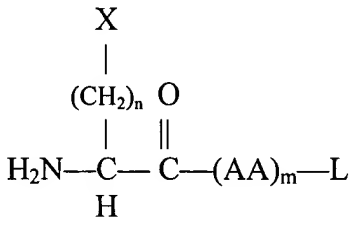
14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

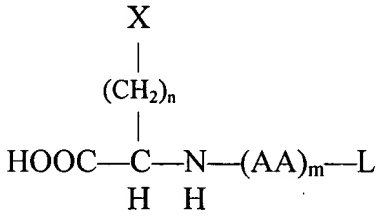
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 12 and 16 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Duschl et al (Reference AT3 on Applicant's PTO-1449).

First, please note that the examiner is interpreting the structures of claim 16 to be as follows:





If applicant intends for the structures to be other than what is represented then the examiner asks for this to be put on the record.

If the terminology in claim 12 of "about 2" (see Paragraph 9D) and in claim 16 of "at least about 2" (see Paragraph 9E) are interpreted as being inclusive of 1 amino acid then Duschl et al anticipates the claims. Duschl et al teach peptide self-assembled monolayers (SAMs) bound in a predetermined pattern having ordered areas where the peptides are and are not bound, as shown in Figure 1B and Figure 3. The patterns are formed by linear peptides containing

a terminal cysteine group and are directly bound to the gold by the interaction of the thiol sidechain with the surface. The peptides have the structure $CY(NANP)_3$ – with C being the terminal reactive group (terminal amino acid), Y the central linker and $(NANP)_3$ the presenting group (see pages 1230-1231) and the structures of the peptides in Duschl et al read directly on the peptides of claim 12 and 16.

If, however, the terminology in claim 12 of "about 2" (see Paragraph 9D) and in claim 16 of "at least about 2" (see Paragraph 9E) are **not** interpreted as being inclusive of 1 amino acid then it would be *prima facie* obvious to modify the peptides of Duschl et al to have a longer linking group. The peptides of Duschl et al form stable monolayers with the single amino acid linker but one of ordinary skill in the art would realize that it is the NANP sequence that possesses the affinity for the target and the length of linker could be modified to modulate monolayer formation or properties.

New Grounds of Rejection
Claim Rejections - 35 USC § 103

17. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Duschl et al or Lopez et al as applied above, in view of Kumar et al (US patent 5,512,131, of record).

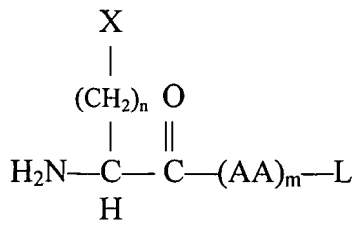
Duschl et al and Lopez et al teach self-assembled monolayers (SAMs) of peptides that are patterned as described above. In both of the references the substrates are gold that has been evaporated onto glass, but neither of the references teach making the SAMs directly on glass substrates. However, it was

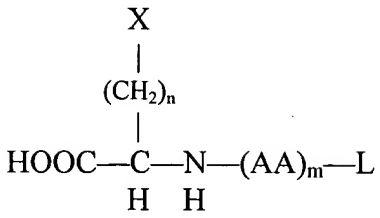
well known in the art at the time of filing that such monolayers could be made directly on glass with the appropriate choice of reactive groups. Kumar et al teach a method of patterning SAMs that is identical to that of the instant invention and teach that "a wide variety of materials and SAM-forming molecular species are suitable", listing silica and glass as some of the preferred materials (see column 10, lines 40-45 and 57-64).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to make the patterned monolayers of Duschl et al or Lopez et al on glass as taught by Kumar et al. One would have been motivated to do so in order to have a transparent substrate material for ease in analysis of the patterned SAMs (and binding partners thereof) as also taught by Kumar et al (column 15 line 66-column 16 line 4).

18. Claims 7 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duschl et al as applied above in view of Wang et al (first author Chaikof, entire article from Mat. Res. Soc. Symp. Proc. Vol. 414, 1996, pp.17-22, of record).

First, please note that the examiner is interpreting the structures of claim 16 to be as follows:





If applicant intends for the structures to be other than what is represented then the examiner asks for this to be put on the record.

For the sake of this rejection, the terminology in claim 12 of "about 2" is interpreted to mean "2" (see Paragraph 9D) and in claim 16 of "at least about 2" is interpreted as meaning "2 or more" (see Paragraph 9E). Duschl et al teach peptide self-assembled monolayers (SAMs) bound in a predetermined pattern having ordered areas where the peptides are and are not bound, as shown in Figure 1B and Figure 3. The patterns are formed by linear peptides containing a terminal cysteine group and are directly bound to the gold by the interaction of the thiol sidechain with the surface (see pages 1230-1231 of the reference). In the structures above, this corresponds to n=1 and X=SH. The structures of the peptides in Duschl et al read directly on the peptides of claim 16 with the exception of the length of the central linker. The peptides have the structure $CY(NANP)_3$ – with C being the terminal reactive group (terminal amino acid), Y the central linker and $(NANP)_3$ the group that binds specifically to a target (L from the instant claim 16). The $(NANP)_3$ moiety is shown to bind an antibody (see Figure 8), which reads on claims 14 and 15. Duschl et al lacks a teaching of the central linker being a beta strand (claim 7) or having two or more amino acids

(claims 12 and 16). Duschl et al also lacks the teaching of the linker being oligoglycine or oligoalanine (claim 13). However, Wang et al teaches monolayers of peptides that are also very similar to the recited structure. They have the presenting group GRGD (L from the instant claim 16) and have and oligo-βalanine before the terminal group of $(CH2)_2SH$. Thus the peptides of Wang et al have a central linker of three amino acids that is an oligoalanine. Wang et al also teach that these linkers are advantageous for forming a β-sheet monolayer structure (see page 19).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to make the patterned monolayers of Duschl et al with peptides having a longer central linking group as taught by Wang et al. One would have been motivated to do so in order to form a β-sheet monolayer structure which is close-packed and has "the potential for both enhanced physiochemical and biological properties" (see page 21 of Wang et al, bottom) that has the additional advantages of a patterned monolayer as taught by Duschl et al (see Discussion, page 1236).

19. Claims 1-3, 6, 8-11 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singhvi et al (Reference AY on Applicant's PTO-1449) in view of Duschl et al as applied above.

Singhvi et al teach a method of patterning SAMs that is identical to that of the instant invention (microcontact printing), making "defined features" with "specific patterns" for placing cells in "predetermined locations and arrays" (see

Abstract). The method is shown in Figure 1 of the reference and produces a solid support that has a patterned monolayer thereon. The pattern comprises regions that are adhesive to proteins and nonadhesive to proteins due to the stamping of hexadecanethiol (adhesive) and then filling in of the non-printed regions with PEG-terminated alkanethiol (nonadhesive) (see page 696). The solid support is exposed to a protein after printing.

Singhvi et al lacks the teaching of forming a peptide monolayer directly by depositing a peptide in the non-printed regions. However, Duschl et al teach patterned peptides directly bound to a gold substrate by the interaction of the thiol sidechain with the surface. The peptides have the structure $CY(NANP)_3$ – with C being the terminal reactive group (terminal amino acid), Y the central linker and $(NANP)_3$ the presenting group (see pages 1230-1231), as shown in Figure 1B and Figure 3. The peptides of Duschl et al are deposited into predefined regions (see Figure 1).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to make the patterned monolayers of Singhvi et al using directly bound peptides to form monolayers in the non-printed regions. One would have been motivated to do so in order to have the advantages of a patterned monolayer structure as taught by Duschl et al (see Discussion, page 1236) utilizing the ease of the stamping techniques as taught by Singhvi et al (see page 698).

Response to Arguments/Amendments

20. The examiner respectfully asks applicant to note that she has cited the "Wang et al" reference on the attached PTO-892 by the correct first author of Chaikof. To avoid confusion, she has continued to refer to this reference as Wang et al in the rejection above but is noting the discrepancy here, for the record.

21. Rejections B and C from the previous Office Action (Paper No. 11, mailed March 30, 1999) are withdrawn in view of applicant's arguments and amendments. Applicant's arguments in the response dated September 1, 1999 (Paper No. 14) and in the Appeal Brief filed February 28, 2000 (Paper No. 18) have been considered but are moot in view of the new ground(s) of rejection. However, the comments below are applicable to the new rejections.

22. As discussed in Paragraph 12 above, applicant's previous response dated January 8, 1999 (Paper No. 8) states the following method:

"... a solid support which will not bind the peptide is coated in a predetermined pattern with a compound that will bind the terminal reactive group of the peptide. The compound is deposited on the solid support in a predetermined pattern using a stamp. Then the solid support is contacted with a solution of the peptide which then binds to the compound in the predetermined pattern."

It appears from applicants response that this methodology is to be included within the scope of the claims, and claims 1, 16, 18 and 19 recites that the peptides are "bound directly" to the substrate. Therefore, the examiner is interpreting the phrase "bound directly" to include peptide monolayers which are bound to the support with no

intermediary species in-between (such as those of Duschl et al) and those which are bound to a compound which in turn is bound to the support (such as those of Lopez et al). This is a very broad interpretation of "bound directly", and the examiner has deemed this to be indefinite since it adds considerable confusion to the claim (see above rejection under 112, second paragraph. Clarification is requested.

Status of Claims/ Conclusion

23. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Kauvar, L. M. US 5,541,070, Issued: 7/30/96; Filed 9/8/93. Discloses coupling of antibodies or fragments thereof to surfaces in predetermined patterns (see claim 9).

Lea et al. Langmuir, January 1992, Vol. 8, pp. 68-73. Teaches the manipulation of proteins into patterns on a mica surface using an AFM tip (see Abstract and Figures).

24. No claims are allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie E. Garcia, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday from 8:30 to 6:00 and alternate Fridays.

26. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Keith MacMillan, can be reached on (703) 308-4614. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie E. Garcia, Ph.D.
May 5, 2000

KEITH D. MacMILLAN
PRIMARY EXAMINER